REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated October 15, 2003.

Status of the Claims

Claims 19-22, 24-27 and 29 are pending in the application.

The §103 Rejections

Claims 19-21, 24 and 29 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Christensen et al [Am. J. Med. Genetics (5/21/1999) vol. 84 (2), pp. 151-157] in view of Steen et al [Prenatal Diagnosis (1998) vol. 18, pp.545-555]. In this new ground of rejection, the Examiner refers to prior remarks that Christensen et al teaches a method of estimating the susceptibility of a pregnant woman to have children with a neural tube defect (NTD) by analyzing nucleic acids and determining the presence of polymorphic alleles of MTHFR and MTR in both mothers and offspring, adding this dataset to a reference (control) dataset, formulates a model based on his combined datasets, and predicts the probability (odds ratio) for any woman to have children with NTDs based on the genetic data, with the Examiner further asserting that Christensen et al teaches measurement of two genetic variables, MTHFR and MTR, and thus suggests adding the MTR genetic variable to his MTHFR data. Steen, the Examiner states, teaches that both MTHFR mutation and vitamin B12 deficiency are independent risk factors for neural tube defects (NTD), wherein a correlation between an MTHFR mutation and spina bifida has been established, as has a correlation between reduced B12 and NTD, and further that the ratio of methionine to folate from maternal amniotic fluid may be indicative of NTD risk. Steen, it is asserted, concludes that both folate and vitamin B12 supplementation would be helpful in reducing the risk of NTD. The Examiner asserts that it would have been obvious to the skilled artisan at the time of the invention to have included the measurements and ratio calculations of Steen in the method of Christensen to genetically discriminate women at risk for having children with NTD. It is further asserted by the Examiner that it would have been obvious to have administered folate and/or vitamin B12

to these women. Applicants respectfully disagree and point out that Christensen determines that MTR has little or negative effect on the probability of a woman having a child with NTD, and his subsequent model does not include MTR data, utilizing only the single gene of MTHFR, or looking at levels of folate cobalamin and MTHFR activity in cases and controls. The combination of Christensen and Steen does not make the invention claimed by applicants obvious. Further, Applicants submit herewith a declaration under 37 C.F.R. 1.131 to overcome the cited Christensen publication, which was published less than one year prior to the date on which the instant application was filed. In view of this, Applicants submit that the Christensen et al reference may not be asserted against the instant invention under 35 U.S.C. 103 and may not be combined with other references in an obviousness rejection.

Claims 19-21, 24 and 29 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Christensen et al [Am. J. Med. Genetics (5/21/1999) vol. 84 (2), pp. 151-157] in view of Steen et al [Prenatal Diagnosis (1998) vol. 18, pp.545-555], as applied to claims 19-21, 24 and 29 above, and further in view of Sarill et al [US 6,274,564 filed 9 /17/1997]. The Examiner asserts that applicants prior arguments with respect to claims 24 and 29 are moot in view of the new ground(s) of rejection. The Examiner notes that claims 24 and 29 as now pending recite a method of lowering the risk of a woman to have offspring with a developmental disorder, as predicted in the method of claim 21, by administering methylfolate, cobalamin, or pyridoxine to the woman. Sarill, it is asserted, teaches periconceptual supplementation with vitamin B12 (which he calls cyanocobalamin) or cobalamin to prevent or decrease the incidence of neural tube defects. The Examiner states that it would have been obvious to one of ordinary skill at the time of the invention to have administered the vitamin B12 or cobalamin of Sarill to women determined to be at risk for having children with NTDs in the method of Christensen and Steen. Applicants respectfully disagree and assert that the combination of Christensen, Steen and Sarill does not make obvious the claimed methods of the invention. As previously pointed out, Christensen does not describe the method of Applicants. In addition, Applicants submit herewith a declaration under 37 C.F.R. 1.131 to overcome the cited Christensen publication, which was published less than one year prior to the date on which the instant application was filed. Therefore, Applicants argue that Christensen may not be asserted against the instant

invention under 35 U.S.C. 103 and may not be combined with other references in an obviousness rejection.

Claims 25-27 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Christensen et al [Am. J. Med. Genetics (5/21/1999) vol. 84 (2), pp. 151-157] in view of Steen et al [Prenatal Diagnosis (1998) vol. 18, pp.545-555], as applied to claims 19-21, 24 and 29 above, and further in view of Scholl [IDS Ref, Am J Clin Nutrition (1996) vol. 63, pp. 520-525]. Scholl, it is noted, teaches monitoring the effect of administering folate to pregnant women, teaches that periconceptual use of folate is known to reduce incidence of NTDs, and teaches that low folate levels are associated with low birth weight and premature delivery. The Examiner remarks that it would have been obvious to the skilled artisan at the time of the invention to have monitored the folate levels of pregnant women, as taught by Scholl, in the method of Christensen and Steen. Applicants respectfully submit that the combination of Christensen, Steen and Scholl does not make obvious the claimed methods. Further, Applicants submit herewith a declaration under 37 C.F.R. 1.131 to overcome the cited Christensen publication - which was published less than one year prior to the date on which the instant application was filed - and argue that Christensen may not be asserted against the instant invention under 35 U.S.C. 103 and may not be combined with other references in an obviousness rejection.

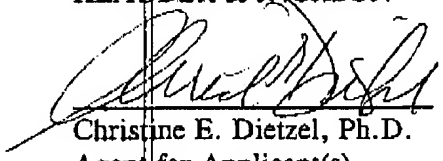
In view of the foregoing remarks, Applicants submit that the Examiner's rejections under 35 U.S.C. 103(a) may properly be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

KLAUBER & JACKSON



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